



## Poikiloderma with neutropenia

Poikiloderma with neutropenia (PN) is a disorder that mainly affects the skin and the immune system. This condition begins with a bumpy rash that usually appears between the ages of 6 and 12 months, gradually spreading from the arms and legs to the torso and face. At about age 2, the rash fades, and the affected child is left with darker and lighter patches of skin coloring (hyperpigmentation and hypopigmentation) and small clusters of blood vessels just under the skin (telangiectases); this combination is known as poikiloderma. Other skin problems include unusually thick skin on the palms of the hands and soles of the feet (palmoplantar keratoderma); calcium deposits that form small nodules (calcinosis cutis), especially on the knees, elbows, or ears; or sores (ulcers) that do not easily heal. Affected individuals also have fingernails and toenails that are thick and abnormally shaped (pachyonychia), fragile teeth, and low bone density.

People with PN have chronic neutropenia, which is a persistent shortage (deficiency) of neutrophils. Neutrophils are a type of white blood cell that plays a role in inflammation and in fighting infection. Neutropenia makes it more difficult for the body to fight off pathogens such as bacteria and viruses. As a result, people with PN experience recurrent sinus infections and pneumonia, especially in the first few years of life. They often develop a condition called bronchiectasis, which damages the passages leading from the windpipe to the lungs (bronchi) and can cause breathing problems. The infections become less frequent after early childhood, but throughout life affected individuals usually have a chronic cough or a reactive airway disease. This term describes asthma and other conditions in which the airways abnormally constrict in response to stimuli such as smoke or a viral infection, leading to wheezing and shortness of breath.

Researchers suggest that PN may increase the risk of cancer, although the level of risk is difficult to determine because only a small number of people have been diagnosed with PN. A type of skin cancer called squamous cell carcinoma, a precancerous blood disorder known as myelodysplastic syndrome (MDS), and a blood cancer called acute myelogenous leukemia that often follows MDS have occurred in a few people with PN.

Some individuals with PN also develop unusual facial features as they grow. These features include a prominent forehead (frontal bossing), widely spaced eyes (hypertelorism), a flat or sunken appearance of the middle of the face (midface hypoplasia), a small nose with a depressed nasal bridge, and a chin that protrudes (prognathism). Short stature and hypogonadotropic hypogonadism (a condition affecting the production of hormones that direct sexual development) can also occur in this disorder.

## Frequency

The prevalence of PN is unknown; only about 100 affected individuals have been described in the medical literature. Although it was first described in the Navajo population of the southwestern United States, it has since been identified in other individuals worldwide.

## Causes

PN is caused by mutations in the *USB1* gene. This gene provides instructions for making an enzyme that functions as an RNA exonuclease. RNA exonucleases cut off (cleave) building blocks called nucleotides one at a time from molecules of RNA (a chemical cousin of DNA). This process helps stabilize the RNA and protects it from damage. Specifically, the USB1 enzyme protects a small RNA molecule called U6, which helps in the assembly of the blueprints for protein production.

Different versions (isoforms) of the USB1 enzyme are produced in different tissues, where they play various roles. In blood-forming tissues, the USB1 enzyme is thought to play a role in the maturation of neutrophils. In the skin, the enzyme is found in pigment-producing cells (melanocytes), cells in the outer layer of the skin called keratinocytes, and structural cells called fibroblasts. Its role in the function of these cells is unknown.

Mutations in the *USB1* gene are thought to lead to an enzyme whose function is impaired. As a result of the dysfunctional USB1 exonuclease, the U6 RNA is not protected from damage. The specific connection between *USB1* gene mutations and the signs and symptoms of PN is unknown. However, the existence of tissue-specific isoforms of the enzyme could help explain why this disorder mainly affects the skin and immune system.

## Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

## Other Names for This Condition

- Clericuzio type poikiloderma with neutropenia
- immune-deficient poikiloderma
- poikiloderma with neutropenia, Clericuzio type

## **Diagnosis & Management**

### Genetic Testing Information

- What is genetic testing?  
[/primer/testing/geneticTesting](#)
- Genetic Testing Registry: Poikiloderma with neutropenia  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1858723/>

### Other Diagnosis and Management Resources

- GeneReview: Poikiloderma with Neutropenia  
<https://www.ncbi.nlm.nih.gov/books/NBK459118>
- Severe Chronic Neutropenia International Registry  
<https://www.scnir-neutropenia.uw.edu/>

## **Additional Information & Resources**

### Health Information from MedlinePlus

- Encyclopedia: Neutropenia -- Infants  
<https://medlineplus.gov/ency/article/007230.htm>
- Health Topic: Immune System and Disorders  
<https://medlineplus.gov/immunesystemanddisorders.html>
- Health Topic: Skin Conditions  
<https://medlineplus.gov/skinconditions.html>

### Genetic and Rare Diseases Information Center

- Poikiloderma with neutropenia  
<https://rarediseases.info.nih.gov/diseases/4085/poikiloderma-with-neutropenia>

### Educational Resources

- Children's Hospital of Chicago: Neutropenia  
<https://www.luriechildrens.org/en/specialties-conditions/neutropenia/>
- Indiana Hemophilia and Thrombosis Center: Chronic Neutropenia  
<https://www.ihtc.org/chronic-neutropenia/>
- MalaCards: poikiloderma with neutropenia  
[https://www.malacards.org/card/poikiloderma\\_with\\_neutropenia](https://www.malacards.org/card/poikiloderma_with_neutropenia)
- Merck Manual Consumer Version: Neutropenia  
<https://www.merckmanuals.com/home/blood-disorders/white-blood-cell-disorders/neutropenia>
- Orphanet: Poikiloderma with neutropenia  
[https://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=221046](https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=221046)

### Patient Support and Advocacy Resources

- British Association of Dermatologists: Skin Support  
<http://skinsupport.org.uk/>
- British Skin Foundation  
<https://www.britishskinfoundation.org.uk/>
- Canadian Skin Patient Alliance  
<https://www.canadianskin.ca/en/>
- Children's Skin Disease Foundation  
<https://www.csdf.org/>
- University of Kansas Genetics Education Center: Dermatology and Genetics  
<http://www.kumc.edu/gec/support/derm.html>

### Clinical Information from GeneReviews

- Poikiloderma with Neutropenia  
<https://www.ncbi.nlm.nih.gov/books/NBK459118>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28poikiloderma+with+neutropenia%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+2520+days%22%5Bdp%5D>

### Catalog of Genes and Diseases from OMIM

- POIKILODERMA WITH NEUTROPENIA  
<http://omim.org/entry/604173>

### Medical Genetics Database from MedGen

- Poikiloderma with neutropenia  
<https://www.ncbi.nlm.nih.gov/medgen/388129>

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